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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/835,298	DAHLEN ET AL.	
	Examiner	Art Unit	
	Ann Y. Lam	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-28,32-34 and 38* is/are pending in the application.

4a) Of the above claim(s) *29-31 and 35-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-28,32-34 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 29-31 and 35-37 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1-22 are canceled.

Claims 23-28, 32-34 and 38 are examined below.

35 USC § 112, 6th Paragraph

The Office notes that the language "means for determining cardiac mortality rate" in claim 23, line 9, and claim 25, line 10, respectively, and "means for determining binding" in claim 23, line 8, and claim 25, line 8, respectively, are being treated under *35 USC § 112, 6th Paragraph.*

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-28, 32-34 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 lines 1-2, recites a "method for predicting cardiac mortality rate in a patient with an acute coronary syndrome". However, the body of the claim does not indicate how the steps allow for prediction of cardiac mortality rate. In other words, it is not clear how cardiac mortality rate is predicted. The limitation "whereby said binding provides a means for determining cardiac mortality rate" is insufficient because it does not indicate how the prediction is made. (Would the mere presence of a marker, i.e., any binding detection, indicate mortality rate? What would the rate be? Would all the markers have to be present? Would the markers have to be above a threshold? What would that threshold be? Or would there just be a comparison between a control? What kind of comparison? What increased level of marker(s) must there be?) For examination purposes, the Office will interpret the preamble to be a method for predicting likelihood of death.

For the same reasons as above, independent claim 25 is vague because it is not clear how the steps allow for prediction of cardiac mortality rate.

Claim 27, lines 1-2, recites a "method for assigning a prognosis to a patient with an acute coronary syndrome" but the claim does not indicate how the prognosis is made. (How is the prognosis assigned? By the mere presence of one marker? Or the mere presence of all the markers? Would the markers have to be above a threshold? What would that threshold be? Or would there just be a comparison between a control? What kind of comparison? What increased level of marker(s) must there be?)

For the same reasons as indicated above, independent claim 33 is vague because it is not clear how the steps allow for assigning a prognosis.

Claims 24, 26, 28, 32, 34 and 38 are rejected under 112, second paragraph because they depend from a claim that is vague as indicated above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 23-28, 32-34 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Jackowski**, [5,290,678], in view of **Antman et al.**, ["Cardiac-specific Troponin I Levels to Predict the Risk of Mortality in Patients with Acute Coronary Syndromes", The New England Journal of Medicine, (1996), pp. 1342-1349, Vol. 335, No. 18], and further in view of **Richards et al.**, ["Neuroendocrine prediction of left ventricular function and heart failure after acute myocardial infarction", Heart, (1999); 81: 114-120].

Jackowski teaches the invention substantially as claimed. Jackowski teaches a multimarker approach comprising the use of antibodies for detecting the presence of at least three markers of cardiac damage in a patient's serum and that the combined responses of reagents indicates the diagnostic condition of the patient (col. 5, lines 17-21, and lines 43-51).

Jackowski teaches that troponin may be one of the markers that may be detected for this purpose (col. 8, lines 28-29). However, Jackowski does not teach detecting the combination of troponin and BNP, nor for the purpose of detecting cardiac mortality.

Antman et al. however teach that cardiac troponin I can be measured by immunoassay using antibodies that recognize cardiac troponin I (see page 1343, left column, last paragraph.) Moreover, Antman et al. teach that cardiac troponin I in blood is an independent risk factor that identifies patients presenting with unstable angina or non-Q-wave myocardial infarction who are at increased risk of death (see page 1347, left col., last paragraph.) Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the multimarker assay taught by Jackowski using cardiac troponin I to predict increased risk of death because Antman et al. teach that cardiac troponin I in blood is an independent risk factor that identifies patients presenting with unstable angina or non-Q-wave myocardial infarction who are at increased risk of death. One of ordinary skill in the art would recognize the medical benefits of detecting increased risk of death.

Moreover, Richards et al. teach that plasma BNP measured within 1 to 4 days of acute myocardial infarction is a powerful independent predictor of death over the subsequent 14 months (see page 114, left column, last paragraph under the heading "*Conclusions*"). Richards et al. collected blood samples from patients (see page 114, right col., last paragraph) and tested for cardiac peptides using an immunoassay (i.e., a binding assay using antibodies), (see page 115, left col., 1st paragraph). The patients in the study had acute myocardial infarction (see table 3 on page 117). Moreover,

Richards et al. teach that adding BNP in a multivariate analyses added additional information in predicting the composite end point of death (see page 118, right column, last paragraph). Richards et al. concluded that stratification of patients into low and high risk groups can be greatly facilitated by plasma BNP measurements and that these could be included in the routine clinical work up of patients following myocardial infarction (see page 119, right column, last paragraph, under the heading "CONCLUSION"). While Richards et al. do not specifically state that the same type of analysis, i.e., radioimmunoassay, as used in the experiment may be performed for clinical analyses, it is understood to be the same type, i.e., immunoassay (which uses antibodies). (Alternatively, it would have been obvious to one of ordinary skill in the art that the same type of assay, i.e., immunoassay, used by Richards et al. in the experiment may be used for clinical analyses because Richards et al. teach that BNP can be detected using immunoassays.)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide BNP as taught by Richards et al. as a marker in the multimarker assay taught by Jackowski modified by Antman et al. for the purpose of predicting cardiac mortality rate in patients with acute myocardial infarction because Richards et al. teach that BNP is a powerful predictor of death in patients with acute myocardial infarction (see page 114, left column, last paragraph under the heading "*Conclusions*") and that adding BNP as a marker to a multivariate analyses added additional information in predicting death (see page 118, right col., last paragraph).

Thus, with respect to independent claims 23, 25, 27 and 33, Richards et al. teach the steps of contacting a sample with a second antibody (i.e., antibodies used in the radioimmunoassay on page 115, left col., 1st paragraph) that specifically binds to a second marker (BNP), (see page 118, right column, 1st full paragraph);

providing means for determining binding between each of said respective markers and each of said respective antibodies (i.e. the radioimmunoassay, page 115, left col., first paragraph),

whereby said binding provides a means for determining cardiac mortality rate (page 118, right col., last paragraph). (As to claims 27 and 33, the prognosis is considered to be cardiac mortality rate, or death.)

As to the following claims, the references teach the limitations as follows.

As to claims 24, 26, 28,and 34, said body fluid is blood (Antman et al., page 1343, left col., 3rd full paragraph; and Richards et al., page 114, right col., last paragraph).

Regarding the preamble in claims 23 and 27, the above method of predicting cardiac mortality rate is performed on a patient that *has* an acute coronary syndrome (see Antman et al., page 1347, left col., last paragraph; and see Richards et al. page 114, left column, last paragraph).

With respect to 32 and 38, the prognosis is considered to be mortality rate or subsequent death (see Antman et al., page 1347, left col., last paragraph; and see Richards et al. page 114, left column, last paragraph.)

Regarding the preamble in claims 25 and 33, while the references teach that the markers may be performed on patients *with* acute coronary syndromes, such as acute myocardial infarction (see above with respect to claims 23 and 27), the references however do not specifically state that the patients were actually *diagnosed* with acute coronary syndromes. However, the references suggest that a method of predicting mortality rate using the markers should be performed on those patients who have been diagnosed with acute coronary syndromes because they suggest the benefits of performing such a method on high risk groups (which would include those that actually have been diagnosed with acute coronary syndrome). For example, Antman et al. teach that the disclosed method of predicting mortality permits the early identification of patients at increased risk of death (page 1348, right column, last paragraph). Moreover, Richards et al. suggest that stratification of patients into low and high risk groups can be greatly facilitated by plasma BNP measurements and that these could be included in the routine clinical work up of patients following myocardial infarction (see page 119, right column, last paragraph).

Response to Remarks

Applicants' affidavits antedating the Newby et al. reference is acknowledged. The new grounds for rejection relies on Jackowski, 5,290,678, as the primary reference, and has an earlier date of March 1, 1994.

Applicants' arguments with respect to the 112th, second paragraph has been considered but are not persuasive. Because Applicants invoke 112th, sixth paragraph, Applicant is not entitled to just any assay step known to one skilled in the art for determining the correlation between a marker and a prognosis. Because Applicants have not recited how cardiac mortality is predicted, the claims are still vague and indefinite.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ann Lam